Risk of Hypertension in Patients with High Insulin Resistance: A Literature Review

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Abstract

Background: Hypertension was ranked as the third debilitating and disabling disease worldwide. It is considered one of the controllable diseases through the control of its risk factors. One of the risk factors that it is not discussed in the literature is insulin resistance

Aim: In this review, we are going to stand on the last research done about the risk of hypertension in diabetic patients. Furthermore, we will assess the studies quality to help direct future research.

Methods: In this study, we reviewed the recent literature to find studies that assess the risk of hypertension in patients with high insulin resistance.

Results: Eight studies fulfilled the inclusion criteria; two types of studies were identified. One that assessed the insulin resistance as a risk for hypertension while the other two studies assessed the effect of insulin resistance on the risk of complication in hypertensive patients. Based on our review, insulin resistance was positively correlated with hypertension and was a significant risk factor for hypertension. For the complications of hypertension, we found that it was linked to the risk of left ventricular dysfunction and cerebrovascular incidents in hypertensive patients.

Conclusion: Based on our results, we found that insulin resistance as a risk factor for hypertension was not researched much. We encourage the research in this topic especially in different races and developing countries as the most studies are conducted in the USA and Korea as the hypertension risk factors differ based on races and area.

Keywords: Hypertension; Insulin Resistance; Fasting Hyperglycemia

Introduction

Hypertension is a worldwide problem that is ranked third for a cause of disability and decreased quality of life [1]. In a recent meta-analysis to analyze the epidemiology of hypertension, they revealed that the prevalence of hypertension is increasing and there are no signs of decreasing incidence.

The estimated total number of people with hypertension in 2000 was 972 million and 333 million in economically developed countries, and 639 million in economically developing countries [2].

Overall, 26.4% of the world's adult population in 2000 had hypertension. It was predicted that 26.1% of women and 29.2% of men were predicted to have hypertension by 2025. The prevalence of hypertension differs based on sex and country of residence [2]. It was found that Latin America and the Carribean had the highest prevalence in men while in women, it was highest in former socialite areas and Asia. However, the difference between both sexes was very small. It was also found that in young ages, men tend to have a higher incidence of hypertension while women have a higher incidence in much older age. This was linked to menopause which affect the hormonal levels of estrogen and progesterone [2].

A cross-sectional study revealed that being male, old age, married, subjects of upper socioeconomic status, illiterate subjects, and retired subjects. Tobacco and alcohol consumption, overweight, obesity, and abdominal obesity were also associated with hypertension [3].

Another study found that a higher level of education, alcohol consumption, current cigarette use, and physical activity was negatively correlated with hypertension. Other risk factors reported in this study were age, male gender, BMI, low education level, nonsmoking, positive family history of selected medical conditions, occupation, and parity [4]. Monroy., *et al.* reported that age and gender were the main predictors of hypertension [5]. Furthermore, they found that other risk factors included diabetes, obesity, smoking, and proteinuria [5].

One of the newly investigated causes of hypertension was insulin resistance. Insulin resistance is defined as insulin-mediated impaired glucose disposal inside the cells. This will result in compensatory hyperinsulinemia [6]. There are many causes of this pathology and was a whole new entity called insulin resistance syndromes [6,7]. The pathology of the condition is mainly due to a defect in post-receptor insulin signaling [6,7]. Obesity and high-fat diet were the most common cause of insulin resistance [6]. Not many studies investigated the effect of insulin resistance on the risk of hypertension. There were two types of studies; one that investigated insulin resistance in normal healthy adults and the other was in obesity and overweight [8-11]. A study found increased insulin levels in healthy adults was significantly associated with hypertension [10]. Not only the insulin resistance was associated with hypertension but was highly correlated with its complications [8,9]. It was found that it increased the risk of cerebrovascular complications [8]. It was also associated with the damaging effect of hypertension on the diastolic function of the left ventricle [9].

Despite the evidence, there is still more need for studies illustrating the mechanism of hypertension due to insulin resistance. In this study, we reviewed the studies in the last ten years to illustrate the directions of new research and what needs to be investigated.

Methods

MEDLINE database was searched for studies in the last 10 years using PubMed. We used the MeSH (Medical Subject Headings) terms for hypertension and insulin resistance. A manual search was conducted searching the references of the included studies and the related studies in PubMed. We also searched systematic reviews for any relevant papers. We only included human studies assessing the aforementioned relationship starting from 2009. We excluded conference papers, reviews, abstract only papers, and books.

Two reviewers independently reviewed the found papers for fulfilling the inclusion criteria.

Results and Discussion

Our search yielded 4120 studies, after the title and abstract screening, only 140 studies were included. Full-text screening produced nine studies that fulfilled our criteria. The eight studies included six studies that investigated the insulin resistance as a cause of hypertension [11-16] and two studies investigated the consequences of hypertension with insulin resistance [8,9] (Table 1).

ID	Country	Study design	Sample size	Hypertension definition	Purpose
Zhang/2019 [8]	China	Retrospective cohort	2849	SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or current use of anti-hy-pertension medication	Consequences of insulin resistance in hypertensive patients
Bamaiyi/2019 [9]	South Africa	Prospective cohort	704	Use of antihypertensive medication or if the mean of the five conventional BP measurements was >140 (systolic BP) or 90 (diastolic BP) mm Hg in those not receiving medication.	Consequences of insulin resistance in hypertensive patients
Park/2014 [13]	Korea	Prospective cohort	25062	SBP/DBP ≥ 140/90 mm Hg or history of HTN or antihypertensive	Insulin resistance as a cause of hypertension
Lytsy/2014 [14]	Sweden	Prospective cohort	1846	SBP/DBP ≥ 140/90mmHg or antihypertensive medication	Insulin resistance as a cause of hypertension
Arshi/2014 [15]	Iran	Prospective cohort	4093	SBP/DBP ≥ 140/90mmHg or antihypertensive medication	Insulin resistance as a cause of hypertension
Xun/2012 [16]	USA	Prospective cohort	3413	SBP/DBP ≥ 140/90mmHg or antihypertensive medication	Insulin resistance as a cause of hypertension
Sung/2011 [10]	Korea	Prospective cohort	10894	SBP/DBP ≥ 140/90mmHg or history of HTN.	Insulin resistance as a cause of hypertension
Levin/2010 [11]	USA	Prospective cohort	3513	SBP/DBP ≥ 140/90mmHg or antihyper-tensive medication + self-report of HTN	Insulin resistance as a cause of hypertension

Table 1: *The characteristics of the included studies.*

Does insulin resistance cause hypertension?

Six studies investigated insulin resistance as a predictor of hypertension. One of the studies measured the serum level of insulin and insulin/glucose ratio in Iranian participants and investigated it as a cause of hypertension [15]. They compared the effect of insulin resistance on hypertension on both sexes. They followed the patients for 8.9 years and regular check-ups were performed every three years. They found that both insulin resistance and insulin glucose ratio was associated with a higher risk of hypertension. Furthermore, stratification of the risk-based on gender. They found that women had a higher risk of insulin resistance-related hypertension. They also found that obesity with increased BMI had a confounding effect on the relationship between hypertension and insulin resistance indicating the possible link between obesity, insulin resistance and hypertension [15].

However, the study had measured HOMA-IR and there were many parameters that were not studied during the follow-up. The study still provides strong evidence due to the large sample size and long follow-up [15].

 A similar prospective cohort study was conducted in the USA, the study followed the patients starting from 1985 and completed throughout the years up to 20 years. They found a positive association between insulin resistance and hypertension in both men and women. Furthermore, they found that obesity and hypertension were equally associated with the risk equal to normal weight population [16].

Another study measured the fasting insulin level in 25062 Korean patients and divided the patients based on the level of fasting insulin into four groups and followed them for five years. The first group fasting insulin level was less than 6.3, the second group was between 6.3 and 8.0, the third group was more than 8 but less than 10.4 and the final group was more than 10.4. They compared between these aforementioned groups. The incidence of hypertension was 13.3% in the first group followed by 15.4% then 17.5% reached up to 23.2% in the fourth group. The study inferred the positive association between both of them [13]. The follow-up duration of the study was considered short compared to the other studies in the review which was considered as a limitation.

A similar study with a short follow-up duration of five years was conducted in Korea. In this study, they could predict the incidence of hypertension through insulin level. They measured HOMA-IR in these patients [10]. The patients were healthy and with normal weight. It was an addition to the previous study results that inferred that body weight may not be associated with the risk of hypertension in high insulin resistance patients. The study adjusted for age, gender, smoking, alcohol use, exercise status, and each component of metabolic syndrome and found that these covariates were not as significant as the insulin resistance. That's why it was considered as the most important risk factor for hypertension. The study faced the same limitation of the previous study as it was only for five years and had measured HOMA-IR instead of insulin level [10].

Levin., *et al.* assessed the risk of hypertension in the diabetic cohort. In this study, they assessed the level of fasting plasma glucose and basal insulin level. They found that it was positively associated with risk of hypertension due to kidney affection and arterial stiffness. They found that this risk was independent of BMI and other diabetes parameters. The study was conducted in the USA and had only 4.7 years of follow-up duration [11].

Another study that collected the data from two large cohorts and performed a meta-analysis of their results [14]. They used the data from the Uppsala Longitudinal Study of Adult Men (ULSAM; www.pubcare.uu.se/ulsam) and the Uppsala Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS; www.medsci.uu.se/pivus). The data included overweight and obese patients who have insulin resistance. In this study, they found that obesity without insulin resistance can cause hypertension [14]. This contradicts with the previous studies that found that insulin resistance was responsible for hypertension even in the presence of obesity.

How does insulin resistance increase the complications of hypertension?

Two studies assessed the effect of insulin resistance on the risk of complication in hypertension. Zhang., *et al.* had divided the cerebral infarcts into two groups based on the size of infarcts. They measured HOMA-IR and other inflammatory parameters. They found the level of HOMA-IR were significantly higher in bigger size infarcts than smaller infarcts. However, the blood pressure was less in this group. They also found that insulin resistance was a prognostic marker for cerebral infarction patients. It was positively correlated with the cerebral infarction size [8].

The other study was conducted in South Africa and assessed the triad relationship between hypertension, insulin resistance and left ventricular diastolic function. They used echocardiography to assess left ventricular function [9]. They assessed left ventricular diastolic function through pulsed-wave Doppler examination of the mitral inflow at rest. They also used tissue Doppler indices (TDI) as well as left atrial volumes (LAV) [9].

Compared to normotensive, the HOMA-IR was significantly associated with diastolic dysfunction in hypertensive patients [9]. It could also be used as a predictor for diastolic dysfunction in hypertensive patients. They also found that HOMA-IR was associated with lateral wall dysfunction. The effect was similar to BMI [9].

Conclusion

The studies that assessed the relation between insulin resistance and hypertension was not studied much in the last ten years. However, based on the included studies, the insulin resistance was positively associated with hypertension and it increased the risk for its complications.

Conflict of Interest

None.

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